

REMARKS

Claims 24-27, 40-44, 47-58, 67-76, 81-84, 86, and 93-94, were previously withdrawn from consideration. These claims, as well as claim 80, have been cancelled without prejudice or disclaimer. Claims 90 and 95 have been amended. Applicants have added no new claims. Claims 17, 46, 59-66, 77-79, 85, 87-92, 95, and 97 are under consideration.

Specification

The Examiner objects to the specification because page 43 of the specification is allegedly not within the appropriate margins. Office Action, pages 2-3, item 2.

Applicants submit a substitute copy of page 43 concurrently herewith.

The Examiner also objects to page 43 under 37 CFR §1.84(m), as allegedly containing black shading. *Id.* The black marking on page 43 are **not** "shading" as the term is used in §1.84(m). According to §1.84(m), "[s]hading is used to indicate the surface or shape of spherical, cylindrical, and conical elements of an object." 37 CFR §1.84(m). The black markings that are not letters on page 43 do not show the shape or surface of an object. They are no more "shading" than the black letters on page 43. They would more appropriately be termed "highlighting." Markings such as this are commonly used in alignments, and are not used to indicate the surface or shapes of objects, but merely to highlight particular portions of a sequence.

Applicants respectfully request withdrawal of the objection to the specification.

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Claim Objections

The Examiner objects to claim 90 for the recitation of "Pfu." Office Action, page 3, section 4. Without acquiescing to the Examiner's argument, claim 90 has been amended to recite "*P. furiosus*," as recommended by the Examiner.

The Examiner objects to claim 95 for the recitation of "nucleic acid that hybridizes to the complement of the nucleotide sequence." *Id.*, section 5. Without acquiescing to the Examiner's argument, claim 95 has been amended to replace the language "nucleotide sequence" with the language "nucleic acid."

Thus, the Examiner's objections to the claims are moot. Applicants respectfully request reconsideration and withdrawal of the objections to the claims.

Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejects claims 17, 46, and 80 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Office Action, pages 3-5, sections 6-10.

Specifically, the Examiner states that claim 17 recites "selected from at least one of," which, the Examiner states, implies that the *P. furiosus* protein may be a combination of proteins, while the preamble implies that the *P. furiosus* protein is a single protein, and not a mixture. *Id.*, section 8.

Applicants respectfully point out that the preamble of claim 17 recites a "composition of matter comprising a protein **complex** possessing nucleic acid polymerase enhancing activity, the complex **comprising a plurality of subunits** wherein at least one subunit is a *P. furiosus* protein selected from at least one of . . ." Thus, the "at least one subunit" may be more than one subunit, permitting a mixture of proteins. Indeed, the embodiment of the claim wherein the protein complex comprises

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more than one of the enumerated proteins is clearly envisioned within the scope of the claim.

Thus, the language of the claim is appropriate for the scope, and is definite under §112, second paragraph. If the Examiner disagrees with this assessment of the meaning of the claim, Applicants respectfully request that the Examiner suggest a wording which preserves the claim scope, but that the Examiner considers allowable under §112, second paragraph.

The Examiner also rejects claim 46 under 35 U.S.C. §112, second paragraph as allegedly indefinite for the recitation of “at least one of SEQ ID NO: 19 and 71.” *Id.*, section 9. Specifically, the Examiner states that the language of the claim implies that the antibody may bind to a protein that comprises both SEQ ID NO: 19 and SEQ ID NO: 71. The Examiner is correct. The language of the claim is designed to include such an antibody that can bind a protein comprising both of the SEQ ID NOS. It also includes antibodies that bind a protein comprising SEQ ID NO: 19. It also includes antibodies that bind a protein comprising SEQ ID NO: 71.

The amendment to claim 46 proposed by the Examiner, that the claim recite an “antibody that binds to a protein having an amino acid sequence comprising at least one of SEQ ID NO: 19 or 71,” would omit from the scope of the claim an antibody that could bind to a protein having an amino acid sequence comprising both SEQ ID NO: 19 and 71.

Thus, the language of the claim is appropriate for the scope of the claim, and definite under §112, second paragraph. Again, if the Examiner disagrees with this assessment of the meaning of the claim, Applicants respectfully request that the

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Examiner suggest a wording which preserves the claim scope, but that the Examiner considers allowable under §112, second paragraph.

Without acquiescing to the Examiner's rejection, and solely to expedite prosecution, claim 80 has been cancelled without prejudice or disclaimer. Thus, the rejection of claim 80 under 35 U.S.C. §112, second paragraph is moot.

Applicants respectfully submit that claims 17 and 46 satisfy the requirements of 35 U.S.C. §112, second paragraph.

Applicants respectfully traverse the §112, second paragraph, rejections and request reconsideration and withdrawal of them.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejects claims 80, 85, 87-92, and 97 as allegedly not described in a way to convey that one had possession of the claimed invention. Office Action, pages 5-8, sections 11-16.

Without acquiescing to the rejection, claim 80 has been canceled without prejudice or disclaimer. Thus the rejection of claim 80 under 35 U.S.C. §112, first paragraph is moot.

The Examiner rejects claim 85 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to convey that not described in a way to convey that one had possession of the claimed invention at the time of filing. Office Action, pages 7-8, section 16.

The Examiner asserts that "[c]laim 85 is directed to a genus of proteins having polymerase enhancing factor activity wherein the proteins comprise the peptide of SEQ ID NO: 73."

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This assertion is incorrect. The Examiner apparently believes that, because there are many variations of proteins which could comprise the amino acid sequence of SEQ ID NO: 73, the claim is to a genus. The Examiner appears distraught that, in addition to comprising the amino acid sequence of SEQ ID NO: 73 and having polymerase-enhancing factor (PEF) activity, a protein of the claimed invention may have other portions of other amino acid sequences that have other functions. These other amino acid sequences and other potential activities do not define claim 85. Nor do these other potential characteristics have any bearing on whether a protein (a) comprises the amino acid sequence of SEQ ID NO: 73, or (b) has polymerase-enhancing factor (PEF) activity. To reject claim 85 on this basis under 35 U.S.C. §112, first paragraph, is analogous to rejecting claims to a machine because it might have other unenumerated devices attached to it.

Because the features which describe the protein in the claim, such as "comprising the amino acid sequence of SEQ ID NO: 73," do not list multiple independent species, such as multiple SEQ ID NOS, claim 85 in this context should be considered a claim to a species. The Examiner's categorization of this claim as a genus claim is clearly erroneous.

As such, possession of the claimed invention at the time of filing may be demonstrated by an actual reduction to practice of the claimed invention. See Manual of Patent Examining Procedure ("MPEP"), §2163.II.3(a). Applicants have repeatedly demonstrated possession of the claimed invention by an actual reduction to practice throughout the specification, e.g., in Examples 8-16 at page 36, line 25 to page 68, line 18.

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Further, even if the claim was considered a generic claim, Applicants still satisfy §112, first paragraph. To demonstrate possession of a claimed invention, “[a]n applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention ....” MPEP, §2163.II.3(a). “For some biomolecules, examples of identifying characteristics include a sequence, structure, .... other identifying characteristics or combinations of characteristics may demonstrate the requisite possession.” In claim 85, the claimed protein has “polymerase-enhancing factor (PEF) activity” and comprises “the amino acid sequence of SEQ ID NO: 73.” See claim 85.

Thus, it is clear that the Applicants had possession of the claimed invention of claim 85 at the time of filing. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

The Examiner rejects claims 80, 85, 87-92, and 97 under 35 U.S.C. §112, first paragraph as allegedly not enabled. Office Action, pages 8-11, items 17-20. Specifically, the Examiner alleges that the specification “does not provide enablement for (1) a composition comprising any protein, (2) a composition comprising a functional analog of the polypeptide of SEQ ID NO: 71, or (3) a composition or protein extract comprising a *T. thermophilis* dUTPase.” *Id.*, item 17.

First, without acquiescing to the Examiner’s argument, and solely to expedite prosecution, claim 80 has been cancelled without prejudice or disclaimer. Thus, the Examiner’s rejection of claim 80 under 35 U.S.C. §112, first paragraph, is moot.

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Claim 85 recites “[a] protein having polymerase-enhancing factor (PEF) activity comprising the amino acid sequence of SEQ ID NO: 73.” Claim 87 recites “[a] PCR enhancing, protein extract comprising purified proteins from *Thermus thermophilis* that possesses dUTPase activity.” Claims 88-92 and 97 ultimately depend from claim 87.

Claims 85, 87-92, and 97, clearly do not claim “(1) a composition comprising **any** protein” or “(2) a composition comprising a functional analog of the polypeptide of SEQ ID NO: 71.” Nowhere do any of these claims have language directed to such limitations as asserted by the Examiner.

Finally, with regard to claims 97-92 and 97, the Examiner alleges that the specification does not enable “(3) a composition or protein extract comprising a *T. thermophilis* dUTPase.” Specifically, the Examiner does not believe that, given the state of the art at the time of filing and the disclosure of the specification, one of skill in the art could isolate the *T. thermophilis* dUTPase. Office Action, page 10, lines 10-15.

More specifically, the Examiner asserts that the specification is silent in regard to (1) the critical structural elements required in a dUTPase and (2) which regions of SEQ ID NO: 71 correlate with dUTPase activity. The Examiner states that, because an epitope against which an antibody may be raised might not correlate to dUTPase activity, the entire venture of finding a dUTPase through an antibody screen is not enabled.

The Examiner does acknowledge that testing a protein for polymerase-enhancing activity does not constitute undue experimentation. Office Action, page 10, lines 1-3.

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Knowing (1) the critical structural elements required in a dUTPase or (2) which regions of SEQ ID NO: 71 correlate with dUTPase activity are not necessary to successfully find a dUTPase in an antibody screen. A protein with dUTPase activity may be selected by binding to an area that is not responsible for the actual dUTPase activity. Further, selection of proteins that do not possess the desired activity are basic problems inherent in any antibody screening process, and do not constitute undue experimentation. Repeated antibody generation when screening for proteins with certain activities is known to those of skill in the art.

The Examiner attempts to belay the Applicants argument by stating that "one could argue that the number of proteins which would be targeted by such antibody may be small, it is noted that protein purification is not trivial in the art and one may require structural information to determine the best chromatography approach to achieve its purification." Office Action, page 11, lines 1-4.

Applicants respectfully point out that, first, purification is not necessary to determine whether a putative protein possesses dUTPase activity. Second, the standard for enablement is not whether a process (such as purification of a dUTPase) would be **trivial**, as asserted by the Examiner, but whether the process would constitute undue experimentation. As protein purification of new, uncharacterized proteins was routine among those of skill in the art at the time of filing (whether or not it was trivial), such a procedure could not constitute undue experimentation. Applicants respectfully assert that isolation of polypeptides, analogs, and protein extracts was routine in the art at the time of filing. See, e.g., specification, page 20, lines 11-13 ("Methods of making extracts of these cells are known in the art ...."); page 47, lines 16-27; and generally

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Ausubel, F.M., et al (1989) Current Protocols in Molecular Biology, Greene Publishing Associates and Wiley-Interscience, New York, NY; Sambrook, J. et al. (1989) Molecular Cloning: A Laboratory Manual, 2<sup>nd</sup> ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.

The Examiner also asserts that the specification "discloses that there is higher structural homology between the polypeptide of SEQ ID NO: 71 and dCTPases than there is with dUTPases." Office Action, page 11, lines 7-9. Whether or not this assertion is true has no bearing on whether claim 87 is enabled. The Examiner has not shown how this has any affect on the ability of one of skill in the art to practice the claimed invention, and thus it cannot be addressed.

Applicants again respectfully reassert, as in their previous Amendment, that the Examiner is applying the enablement test incorrectly. As long as the specification discloses at least one method of making the invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied. MPEP § 2164.01 (b). "Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. 112." *Id.*

Again, Applicants point to *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988), where the court reversed a finding of lack of enablement under §112, first paragraph. See MPEP §2164.06(b), under "Several Decisions Ruling That The Disclosure Was Enabling." The nature of the invention in that case involved the generation of monoclonal antibodies, and then screening the monoclonal hybridomas to determine which monoclonals possessed the desired characteristics. Although one of

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skill in the art could not predict the structure of all antibodies that would fit the claimed invention in that case, the court found that the specification was sufficient to allow one of skill in the art to determine which antibodies possessed the desired characteristics, and thus fell within the scope of the claims. Thus, the specification in *In Re Wands* was found to be enabling for monoclonal antibodies, the structure of which were not necessarily predictable.

Thus, the Examiner has failed to establish that claims 85, 87-92, and 97 are not enabled under 35 U.S.C. §112, first paragraph. Thus, Applicants respectfully traverse the §112, first paragraph, rejections of those claims and requests reconsideration and withdrawal of them.

Rejection Under 35 U.S.C. §102(a)

The Examiner rejects claim 80 under 35 U.S.C. § 102 as allegedly anticipated by Cohen, et al., (Genomics 40(1):213-215, 1997; GenBank accession number U62891 (DNA) ("U62891"); and AAC51123 (protein)) ('Cohen'). Office Action, page 11, section 21. Specifically, the Examiner states that "[c]laim 80 is drawn to a composition comprising any protein including functional analogs of the polypeptide of SEQ ID NO: 71." The Examiner reasons that because "Cohen et al. teaches a human dUTPase (dUTP pyrophosphatase) which has polymerase enhancing activity," Cohen must anticipate claim 80.

Without acquiescing to the rejection, and solely to expedite prosecution, Applicants have cancelled claim 80. Thus, the rejection under 35 U.S.C. §102(a) is

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moot. Applicants request reconsideration and withdrawal of the rejection under 35 U.S.C. §102.

Double Patenting

The Examiner rejects all considered claims as allegedly being unpatentable over claims of U.S. Patent No. 6,183,997, to Hogrefe ("Hogrefe") under the nonstatutory judicially created doctrine of obviousness-type double patenting. Office Action, page 12, sections 22 -24.

Without acquiescing to the rejection, if the claims are otherwise found in condition for allowance, the Applicants will file a terminal disclaimer.

Conclusion

Applicants request the timely allowance of the application. In the event the Examiner does not find the claims allowable, Applicants request that the Examiner contact the undersigned at (650) 849-6676 to set up an interview.

Please grant any extensions of time required to enter this Amendment and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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